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(54) Title: USE OF A PROTEASOME INHIBITOR IN THE TREATMENT OF ENDOTHELIAL DYSFUNCTION AND/OR IN A LOW-DOSE PROTEASOME INHIBITOR THERAPY

(57) Abstract: The present invention relates to the use of a proteasome inhibitor for the manufacture of a medicament for the prevention, onset therapy, acute therapy and/or regression of diseases associated with endothelial dysfunction. The present invention also relates to the use of a proteasome inhibitor as a low-dose treatment.

WO 2004/012732 A3

INTERNATIONAL SEARCH REPORT

International Application No
PCT/EP 03/08495

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A61K31/4015 C07D207/46 C07D263/14 A61K38/06 A61P9/10

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 A61K C07D

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal, WPI Data, PAJ, BIOSIS, MEDLINE, EMBASE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 01/047540 A (BETH ISRAEL HOSPITAL) 5 July 2001 (2001-07-05) *cf. abstract, page 7, lines 19-25, page 8, line 23 bridging with page 9, line 24, experiment 2 on pp. 46/47, claims 1/4/5*	1-10, 13-24
X	WO 99/09006 A (BEHNKE MARK ;ROUSH WILLIAM (US); PLAMONDON LOUIS (US); SOUCY FRANC) 25 February 1999 (1999-02-25) *cf. abstract, page 9, line 15 bridging with page 10, line 2, page 31, line 2, page 41, lines 3-9, example 15 on page 67ff., page 69, lines 1-5, claims 71/72*	1-10, 13-24

☐ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

° Special categories of cited documents :

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"O" document referring to an oral disclosure, use, exhibition or other means

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"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

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Date of the actual completion of the international search	Date of mailing of the international search report
17 December 2003	12 03. 2004

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Stoltner, A

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This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-10, 13-24 (PART)

Use of at least on proteasome inhibitor for the manufacture of a medicament for the prevention, onset therapy, acute therapy and/or regression of diseases "associated with endothelial dysfunction", wherein the proteasome inhibitor is selected from a group comprising:

a) naturally occurring proteasome inhibitors comprising peptide derivatives which have a C-terminal epoxy keton structure, beta-lacton-derivatives, aclacinomycin A, lactacystin, clastolactacystin.

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2. claims: 1-10, 13-24 (PART)

Use of at least on proteasome inhibitor for the manufacture of a medicament for the prevention, onset therapy, acute therapy and/or regression of diseases "associated with endothelial dysfunction", wherein the proteasome inhibitor is selected from a group comprising:

b) synthetic proteasome inhibitors comprising: modified peptide aldehydes such as N-carbobenzoxy-L-leucinyl-L-leucinyl-L-leucinal (MG132), or the boric acid derivative of MG232, N-carbobenzoxy-Leu-Nva-H (MG115), N-acetyl-L-leucinyl-L-leucinyl-L-norleucinal (LLnL), N-carbobenzoxy-Ile-Glu(OBut)-Ala-Leu-H (PS1).

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3. claims: 1-10,13-24 (PART)

Use of at least on proteasome inhibitor for the manufacture of a medicament for the prevention, onset therapy, acute therapy and/or regression of diseases "associated with endothelial dysfunction", wherein the proteasome inhibitor is selected from a group comprising:

c) peptides comprising: an alpha,beta-epoxyketone-structure, vinyl-sulfones such as carbobenzoxy-L-leucinyl-L-leucinyl-L-leucin-vinyl-sulfon or 4-hydroxy-5-iodo-3-nitrophenylacetyl-L-leucinyl-L-leucinyl-L-leucin-vinyl-sulfon (NLVS).

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4. claims: 1-10, 13-24 (PART)

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INTERNATIONAL SEARCH REPORT

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